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Case Report

# Long-term clinical and radiological outcomes of Copenhagen syndrome with 19 affected levels: a case report

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**Abstract**

**BACKGROUND CONTEXT:** Copenhagen syndrome, or progressive noninfectious anterior vertebral fusion, is a rare disorder of unknown etiology that usually presents with thoracolumbar kyphosis in childhood. There have been no long-term reports on outcome in children with multiple affected levels with longitudinal imaging from infancy to adulthood.

**PURPOSE:** The purpose of this study was to report the long-term outcome of nonoperative management of a child with Copenhagen syndrome affecting 19 vertebral levels.

**STUDY DESIGN:** This study is a case report.

**METHODS:** The study included longitudinal clinical and radiological follow-ups.

**RESULTS:** A 1-year-old female presented with thoracolumbar kyphosis. Plain radiographs and magnetic resonance imaging demonstrated kyphosis associated with anterior disc space narrowing plus T11–T12 and L2–L3 vertebral end-plate abnormalities. Initial treatment with a plaster jacket followed by brace failed to prevent progressive vertebral involvement and kyphosis during childhood. At skeletal maturity, no further levels became involved, and progression was halted. In total, 19 levels showed anterior fusion.

**CONCLUSIONS:** This case describes the long-term outcome of nonoperative management for progressive noninfectious anterior vertebral fusion affecting multiple levels. Extensive vertebral involvement does not always require surgical intervention. There is a need for future research on the prognostic indicators for progression and long-term outcome. 

*Keywords:* Spine; Copenhagen syndrome; Kyphosis; Outcome; Progressive noninfectious anterior vertebral fusion; Radiology; Magnetic resonance imaging

## Introduction

Progressive noninfectious anterior vertebral fusion (PNAVF) is a rare disorder affecting young children. It is eponymously known as Copenhagen syndrome after a 26-patient case series reported at the University Hospital of Copenhagen [1]. Progressive noninfectious anterior vertebral fusion was first described in 1931 by Mosenthal [2], and it is estimated that there are now 80 reported cases [1]. Some of these cases described in historic non-English articles could possibly have been misdiagnosed as Scheuermann disease.

We performed a systematic review on Pubmed as of October 23, 2014. We searched for the following terms: ''noninfectious vertebral fusion,'' ''spontaneous anterior vertebral fusion,'' ''progressive anterior vertebral fusion,'' and ''Copenhagen disease.'' The search returned 593 articles, and 2 reviewers assessed inclusion criteria based on the accuracy of diagnosis of PNAVF. Sixteen articles were identified that reported the condition including a total of 65 cases of PNAVF [1,3–17].

Progressive noninfectious anterior vertebral fusion presents in early childhood with kyphosis and tends to progress rapidly during adolescence. The deformity is thought

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to stabilize in early adulthood once fusion is complete [1]. The cause remains unknown. It has been postulated that a congenital etiology [1,5] or exposure to prenatal substances like thalidomide might be causative [1,6], although this has never been proven.

The first radiological features that occur shortly after birth include anterior irregularity in involved vertebral body end plates [14]. The anterior part of the disc space narrows and progresses to complete bony ankylosis [6,14]. Posteriorly, the disc is relatively spared in the early stages. Magnetic resonance imaging demonstrates end-plate edema in the anterior discovertebral margins, which precede radiographic changes. Magnetic resonance imaging does not currently provide prognostic information [14].

It is thought that kyphosis is proportional to the number of affected discs and extent of fusion affecting these disc spaces [1]. Treatment involves bracing during childhood to slow progression [1] or surgical correction of deformity [14]. There have been few reports of the syndrome with long-term follow-up, and it is unclear whether more severely affected children, with greater number of affected levels, can be successfully treated by observation and brace treatment. The largest case series involving 26 children described a mean progression of kyphosis from 25.5 to 37.7 over a mean of 13.3 years. Nine of these children were treated by brace alone, of whom six demonstrated improvement in kyphotic alignment [1]. Most case studies report outcome in children with less than 5 affected levels, and we could find no reports involving children with more than 11 affected levels. This case reports outcome of a child with 19 affected levels treated nonoperatively over 20 years.

## Case report

A 1-year-old female presented with thoracolumbar kyphosis that had been noticed by the parents. History included hypotonia and mild motor developmental delay. There was no family history of spinal deformity, and obstetric history was unremarkable. On examination, there was a thoracolumbar kyphosis with the evidence of mild generalized hypotonia. Local ethical approval was obtained, and the study was performed following the Declaration of Helsinki principles with consent obtained from the study subject.

Radiographs demonstrated anterior narrowing at the T11–T12 and L2–L3 disc spaces anteriorly with a kyphosis measuring 62° (Fig. 1, Left). Magnetic resonance imaging showed anterior disc height loss at these levels with high signal intensity at multiple end-plate levels, thought to represent normal physeal appearances at this age (Fig. 1, Right). Nonoperative management was started with four serial plaster jackets changed every 10 weeks, followed by a thoracolumbar-sacral orthosis worn for 23 hours a day.

During subsequent follow-up with brace treatment, the child remained asymptomatic, and the degree of kyphosis decreased to 54°. Between the ages of 10 to 12 years, despite bracing, the deformity started to progress with further levels becoming involved. Radiographs at the age of 12 years showed anterior fusion at multiple levels extending between T9–L1 and L2–L5. The kyphotic deformity had increased to 76° (Fig. 2, Left). Magnetic resonance imaging confirmed solid fusion and showed anterior disc narrowing between these levels with evidence of fatty marrow replacement in several vertebrae. The fusion had also involved the posterior elements at several levels (Fig. 2, Right).

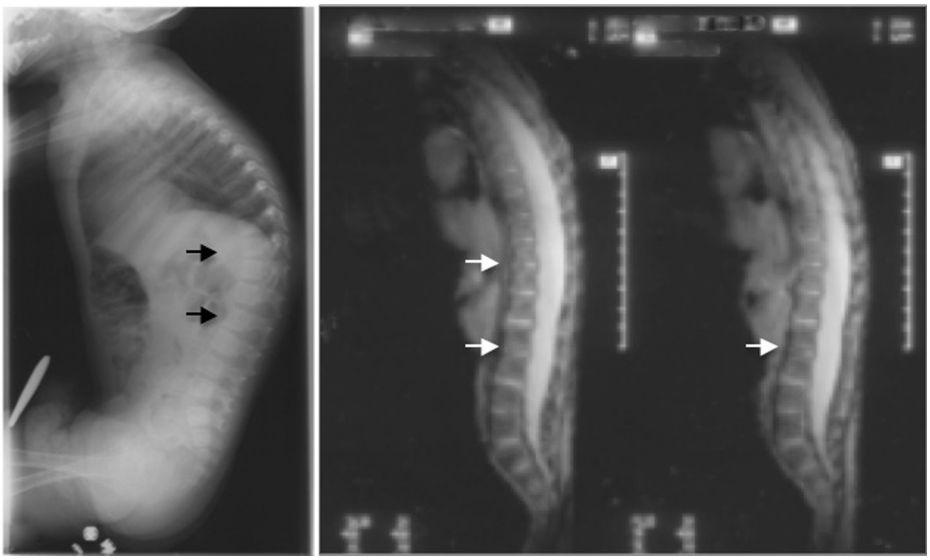

Fig. 1. (Left) Lateral whole spine radiograph at 12 months of age, demonstrating loss of anterior disc space height and end-plate irregularity at the T11–T12 and L2–L3 levels (black arrows). (Right) Sagittal short tau inversion recovery magnetic resonance imaging at 12 months of age of the thoracolumbar spine showing symmetrical disc space narrowing (white arrows). The high signal intensity horizontally at multiple end-plate levels was considered a normal physeal appearance at this age.